In cord blood bank practice, the 6 obstetric factors given above and CBU weight are generally known before the decision on further processing is made. In the respective regression model with TNC as dependent variable, the highest absolute β values were reached for CBU weight ($\beta = 0.70$) and vaginal delivery ($\beta = 0.33$) followed by the number of preceding pregnancies (β=-0.13). These factors were also significant at $p = 0.05$.

The presented data can be applied to optimize cord blood bank operations. As one result one could, for example, establish different CBU minimum weights for further processing subject to birth route: since CBUs from vaginal deliveries have higher WBC counts, the respective minimum weight could be lower than that of CBUs from sectios.

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DOUBLE UMBILICAL CORD BLOOD TRANSPLANTATION ACHIEVES UNIVERSAL ENGRAFTMENT BUT IS ASSOCIATED WITH CONSIDERABLE TRANSPLANT-RELATED MORTALITY

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The applicability of umbilical cord blood transplantation (UCBT) is limited by inadequate cell dose especially for adult patients. Infusion of 2 partially HLA-matched units has been shown to facilitate engraftment, and allows for transplantation of patients for whom a single unit of sufficient cell dose is not available. However, double UCBT is associated with an increased risk of acute graft-versus-host disease (aGVHD), which may impair the outcomes. From 8/2006 to 7/2009, 21 patients (female:male = 10:11) with high-risk acute myeloid (AML, n = 16) or lymphoblastic (ALL, n = 5) leukemia received double UCBT in our center. The patients had a median age of 36 years (range: 16-60), and a median weight of 75 kg (range: 53-105). The median time from diagnosis to UCBT was 10 months (range: 3-91). The disease phase at transplant was 1st complete remission (CR1) in 10 patients, CR2 in 5, and ≥CR3 or resistant relapse in 6. The conditioning regimen was myeloablative in 16 (TBI-based: 7, busulfan-based: 9), and reduced-intensity in 5 patients. ATG was administered during conditioning only in 1 patient. Cyclosporine plus mycophenolate mofetil was used for aGVHD prophylaxis. The majority of UCB units (34/42) were 4/6 antigen matched to recipient at HLA-A, -B, and -DRB1. The median total doses of nucleated and CD34+ cells at infusion were 4.3 × 10^7/kg (range: 2.65-5.4 × 10^7/kg) and 1.33 × 10^5/kg (range: 0.6-3.1 × 10^5/kg), respectively. Neutrophil recovery was achieved in all but 1 patient at a median of 19 days [cumulative incidence (CI) by day 52, 95%]. The CI of platelet recovery (>50,000/uL) was 62% by day 270, and occurred at a median of 83 days (range: 32-193). Eighteen patients (CI, 85%) developed aGVHD (grade II-IV: 18, III-IV: 5). Three of 12 evaluable patients, who survived for more than 100 days, developed chronic GVHD (CI, 14%). Treatment-related mortality (TRM) was 38% at day 100 and 52% at 1 year. Causes of TRM were infection (n = 6), GVHD (n = 3), and transplant-associated microangiopathy (n = 2). Disease relapse occurred in 5 patients (CI, 28.5% at 1 year). The 2-year disease-free and overall survival is 24% and 28%, respectively. Five patients are alive and in CR, 10-38 months after UCBT. In conclusion, double UCBT results in an excellent rate of engraftment in adult recipients. However, further improvements should focus on the reduction of early TRM, which is significantly high and might be attributed to the increased incidence of aGVHD.

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FLUDARABINE, CYCLOPHOSPHAMIDE AND ANTITHYMOCYTE GLOBULIN (ATG) AS CONDITIONING REGIMEN IN MATCHED RELATED AND UNRELATED ALLOGENEIC STEM CELL TRANSPLANTATION FOR SEVERE APLASTIC ANEMIA (SAA): THE M.D. ANDERSON CANCER CENTER TEN-YEAR EXPERIENCE

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Background: Total body irradiation (TBI) is often employed in matched unrelated donor (MUD) allogeneic stem cell transplantation (allo-SCT) in SAA. However, even at low doses, TBI can cause serious short- and long-term toxicities. In matched related donors (MRD), outcome in SAA patients ≥ 40 years with high-dose cyclophosphamide (CY) ± ATG is poor due to graft rejection, GVHD and organ failure. **Aim**: To explore feasibility of a fludarabine (FLU)–based, high-dose ATG, TBI-free regimen in MUD (all ages) and MRD (recipient > 40 years) allo-SCT.

Methods: Over a 10-year period (1999-2009), twenty SAA patients underwent allo-SCT with a FLU-CY-ATG regimen from a MRD (n = 7, all age ≥ 40) or a MUD (n = 13, any age). Median age was 34 years (range 1-59). Seven pts (33%) were ≥ 50 years old. Bone marrow was used as SC source in all but four patients. Once the regimen was standardized, it included (n = 13) FLU (30 mg/m sq × 4 days) intravenously (IV), CY (300 mg/m sq IV × 4 days), and thymoglobulin (THY, 3.75 mg/kg IV × 3-4 days). Before that, in seven patients doses were FLU 20-50 mg/m sq IV × 4 days; CY 40-60 mg/kg IV × 2-4 days; ATG IV 20-30 mg/kg (horse product) or 3 mg/kg (THY) x 2-4 days. Median time from diagnosis to allo-SCT was 12 months (2-244). Eleven patients (55%) were transplanted off study (active infection, poor organ function, etc).

Results: Seventeen out of 19 evaluable patients engrafted (90%). There were two secondary graft failures (10%). Median time to neutrophil recovery (i.e. absolute neutrophil count ≥ 500/mL) was 15 days (range 8-30). Chimerism studies indicated ≥90% donor-derived engraftment in 16/19 evaluable patients (75%) and thirteen patients were 100% donor. Four out of 20 evaluable patients (20%) developed acute grade II-IV GVHD, and 6/16 evaluable patients (37%) developed chronic GVHD. Thirteen patients (62%) are alive (including eight out of the last nine treated) with a median follow-up of 30 months (3-112). Seven patients expired (graft rejection n = 1, infection n = 2, GVHD n = 1, organ failure n = 1, EBV lymphoproliferative disorder/LPD n = 2). There was one early death (death < day +30) and no known late graft failures.

Conclusion: Fludarabine-based, TBI-free for MRD and MUD allo-SCT is feasible in this high-risk group (older age, active infection, poor organ function, etc), with high engraftment rates and low early mortality. Presumably due to high-dose ATG, GVHD-related incidence and mortality were low, although EBV LPD was a drawback.

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MULTIPLE UNIT UMBILICAL CORD BLOOD TRANSPLANTATION (MU UCBT) WITH TOTAL BODY IRRADIATION, ETOPOSIDE AND ANTITHYMOCYTE GLOBULIN FOR ADULT HEMATOLOGIC MALIGNANCY PATIENTS

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MU UCBT is an alternative donor transplant approach for adult hematologic malignancy (HM) pts. TBI and VP16 is an effective conditioning regimen, but its utility in MU UCBT is not well known. From 10/03-2/09 we enrolled 16 adult HM pts on a trial with this regimen prior to MU-UCBT. Eligibility included lack of an HLA matched related or unrelated donor. Pts had to have at least a 4/6 HLA matched UCB unit with at least 0.5×10^7 nucleated cells/kg and a 2nd UCB unit with at least a 4/6 HLA match to the 1st UCB unit. The minimum required cryopreserved TNC dose for both units was 1×10^7/kg or an infused CD34+ cell dose of 1.5×10^5/kg. Pts received TBI 1,320 cGy (days -7 to -4), VP16 60 mg/kg (day -3) and ATG 30 mg/kg (days -3 to +1). GVHD prophylaxis: tacrolimus and mycophenolate. Median age was 47 yrs (range, 18-60) and diagnoses were 8 AML, 3 CML, 2 MDS, 1 ALL, 1 CLL 1 NHL. Median time from diagnosis to UCBT was 8 mos. The 1st UCB unit infused (UCB1) included five 4/6, ten 5/6 and one 6/6 HLA matches with the recipient, and for the 2nd UCB unit (UCB2) with recipient there were one 3/6, five 4/6, and ten 5/6 matches. Median thawed TNC doses infused for UCB1 and UCB2 were 1.6×10^7/kg and 1.2×10^7/kg, respectively; thawed CD34+ cell doses were 0.6×10^5/kg for both units.12 were evaluable for engraftment; 3 others